

CLAIMS:

1. An isolated nucleic acid sequence, of an alternative splicing variant, selected from the group consisting of:
 - (i) the nucleic acid sequence depicted in any one of SEQ ID NO: 1 to 5 SEQ ID NO: 36;
 - (ii) nucleic acid sequences having at least 90% identity with the sequence of (i) with the proviso that each sequence is different than the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing; and
 - 10 (iii) fragments of (i) or (ii) of at least 20 b.p., provided that said fragment contains a sequence which is not present, as a continuous stretch of nucleotides, in the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing.
2. An isolated nucleic acid sequence complementary to the nucleic acid 15 sequence of Claim 1.
3. An amino acid sequence selected from the group consisting of:
 - (i) an amino acid sequence coded by the isolated nucleic acid sequence of alternative splice variants of Claim 1;
 - (i) homologues of the amino acid sequences of (i) in which one or more 20 amino acids has been added, deleted, replaced or chemically modified in the region or adjacent to the region where the amino acid sequences differs from the original amino acid sequence, coded by the original nucleic acid sequence from which the variant has been varied.
- 25 4. An amino acid sequence according to Claim 3, as depicted in any one of SEQ ID NO: 37 to SEQ ID NO: 72.
5. An isolated nucleic acid sequence coding for any one of the amino acid sequences of Claim 3.
6. A purified antibody which binds specifically to any one of the amino acid 30 sequence of Claim 3.

7. An expression vector comprising any one of the nucleic acid sequences of Claim 1 and control elements for the expression of the nucleic acid sequence in a suitable host.

8. An expression vector comprising any one of the nucleic acid sequences of 5 Claim 5 and control elements for the expression of the nucleic acid sequence in a suitable host.

9. An expression vector comprising any one of the nucleic acid sequences of Claim 2, and control elements for the expression of the nucleic acid sequences in a suitable host.

10. A host cell transfected by the expression vector of Claim 7.

11. A host cell transfected by the expression vector of Claim 8.

12. A host cell transfected by the expression vector of Claim 9.

13. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:

15 (i) the expression vector of Claim 7; and
(ii) any one of the amino acid sequences of Claim 3.

14. A pharmaceutical composition according to Claim 13, for treatment of diseases which can be ameliorated or cured by raising the level of any one of the amino acid sequences depicted in SEQ ID NO: 37 to SEQ ID NO: 72.

20 15. A pharmaceutical composition according to Claim 14, for the treatment of cancer.

16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:
25 (i) any one of the nucleic acid sequences of Claim 2;
(ii) the expression vector of Claim 9; and
(iii) the purified antibody of Claim 6.

17. A pharmaceutical composition according to Claim 14, for treatment of diseases which can be ameliorated or cured by decreasing the level of any one of the amino acid sequences depicted in SEQ ID NO: 37 to SEQ ID NO: 72.

30 18. A pharmaceutical composition according to Claim 17, for the treatment of cancer.

19. A method for detecting an variant nucleic acid sequence in a biological sample, comprising the steps of:

(a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1; and

5 (b) detecting said hybridization complex;

wherein the presence of said hybridization complex correlates with the presence of an variant nucleic acid sequence in the said biological sample.

20. A method for detecting an variant nucleic acid sequence in a biological sample, comprising the steps of:

10 (a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 2; and

(b) detecting said hybridization complex;

wherein the presence of said hybridization complex correlates with the presence of an variant nucleic acid sequence in the said biological sample.

15 21. A method for determining the level of variant nucleic acid sequences in a biological sample comprising the steps of:

(a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1; and

20 (b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the variant nucleic acid sequences in the sample.

22. A method for determining the level of variant nucleic acid sequences in a biological sample comprising the steps of:

(a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 2; and

(b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the variant nucleic acid sequences in the sample.

23. A method for determining the ratio between the level of variant of the 30 nucleic acid sequence in a first biological sample and the level of the original

sequence from which the variant has been varied by alternative splicing in a second biological sample comprising:

- (i) determining the level of the variant nucleic acid sequence in the first biological sample according to the method of Claim 21;
- 5 (ii) determining the level of the original sequence in the second biological sample; and
- (iii) comprising the levels obtained in (a) and (b) to give said ratio.

24. A method for determining the ratio between the level of variant of the nucleic acid sequence in a first biological sample and the level of the original 10 sequence from which the variant has been varied by alternative splicing in a second biological sample comprising:

- (iv) determining the level of the variant nucleic acid sequence in the first biological sample according to the method of Claim 22;
- 15 (v) determining the level of the original sequence in the second biological sample; and
- (vi) comprising the levels obtained in (a) and (b) to give said ratio.

25. A method according to Claim 23, wherein said first and said second biological samples are the same sample.

26. A method according to Claim 24, wherein said first and said second 20 biological samples are the same sample.

27. A method according to Claim 19, wherein the nucleic acid material of said biological sample are mRNA transcripts.

28. A method according to Claim 20, wherein the nucleic acid material of said biological sample are mRNA transcripts.

25 29. A method according to Claim 27, where the nucleic acid sequence is present in a nucleic acid chip.

30. A method according to Claim 28, where the nucleic acid sequence is present in a nucleic acid chip.

31. A method for detecting a variant nucleic acid sequence in a biological 30 sample comprising the steps of:

(i) contacting the sample primer for amplifying with any one of the nucleic acid sequences of SEQ ID NO: 1 to SEQ ID NO: 36;

(ii) contacting the sample with reagents for nucleic acid amplification and under conditions enabling nucleic acid amplification;

5 (iii) detecting the presence of amplified sequences, said presence correlates with the presence of any one of SEQ ID NO: 1 to SEQ ID NO: 36 in the sample.

32. A method for detecting any one of the amino acid sequences of Claim 3 in a biological sample, comprising the steps of:

10 (a) contacting with said biological sample the antibody of Claim 6, thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex
wherein the presence of said antibody-antigen complex correlates with the presence of the desired amino acid in said biological sample.

15 **33.** A method for detecting the level of the amino acid sequence of any one of Claim 3 in a biological sample, comprising the steps of:

(a) contacting with said biological sample the antibody of Claim 6, thereby forming an antibody-antigen complex; and

(b) detecting the amount of said antibody-antigen complex and
20 normalizing said amount to provide the level of said amino acid sequence in the sample.

25 **34.** A method for determining the ratio between the level of any one of the amino acid sequences of Claim 3 present in a first biological sample and the level of the original amino acid sequences from which they were varied by alternative splicing, present in a second biological sample, the method comprising:

(i) determining the level of the amino acid sequences of Claim 3 into a first sample by the method of Claim 33;

(ii) determining the level of the original amino acid sequence in the second sample; and

30 (iii) comparing the level obtained in (a) and (b) to give said ratio.

35. A method according to Claim 34, wherein said first and said second biological samples are the same sample.

36. A method for detecting any one of the antibodies of Claim 6 in a biological sample comprising the steps of:

5 (a) contacting said biological sample with any one of the amino acid sequences of Claim 3 thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the presence of the antibody in said biological sample.

10 37. A method for detecting the level of any one of the antibodies of Claim 6 in a biological sample comprising the steps of:

(i) contacting said biological sample with any one of the amino acid sequences of Claim 3;

(ii) detecting the amount of said antibody-antigen complex and
15 normalizing said amount to provide the levels of said antibody in the sample.

38. A method for determining the level of the nucleic acid sequences in a biological sample comprising the steps of:

(a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1; and

20 (b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the variant nucleic acid sequences in the sample.

39. A method for determining the ratio between the level of variant of the nucleic acid sequence in a first biological sample and the level of the original
25 sequence from which the variant has been varied by alternative splicing in a second biological sample comprising:

(a) determining the level of the variant nucleic acid sequence in the first biological sample according to the method of Claim 38;
30 (b) determining the level of the original sequence in the second biological sample; and

(c) comprising the levels obtained in (a) and (b) to give said ratio.

40. A method according to Claim 39, wherein said first and said second biological samples are the same sample.